

A light-driven molecular machine based on stiff stilbene

Yuan Wang,^{a,c} Yancong Tian,^b Yu-Zhe Chen,^c Li-Ya Niu,^a Li-Zhu Wu,^c Chen-Ho Tung,^c Qing-Zheng Yang^{*a} and Roman Boulatov^b

We report a new molecular design for optically triggered nm-scale translation of a submolecular component relative to another. We used a rotaxane-like molecule terminated at one end with stiff stilbene that served both as a chromophore to trigger the translation of the pillar[5]arene “wheel” and as a stopper to prevent its dethreading.

^aKey Laboratory of Radiopharmaceuticals, Ministry of Education, College of Chemistry, Beijing Normal University, Beijing 100875, P. R. China. Email: qzyang@bnu.edu.cn

^bDepartment of Chemistry, University of Liverpool
Crown Street, Liverpool L69 7ZD, UK

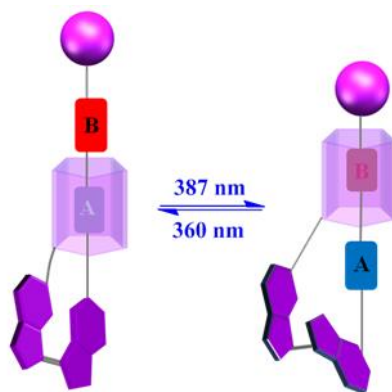
^cKey Laboratory of Photochemical Conversion and Optoelectronic Materials, Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing 100190, P. R. China

Electronic Supplementary Information (ESI) available: synthesis and characterization of compounds **Z-1**, **E-1** and **2-5**, photoisomerization of molecular machine, quantum-chemical calculations, etc.

Molecular machines are “systems where a stimulus triggers the controlled, relatively large amplitude motion of one molecular or submolecular component relative to another”.¹ An important category of molecular machines are switches, which exist in at least two distinct isolable molecular geometries interconvertible upon energy input.²⁻⁵ Although switches lack the asymmetry required to generate work, they constitute a useful platform to test new molecular architectures for converting external stimuli into large conformational rearrangements and to evaluate elementary reaction steps and types of chemical interactions that may be useful for subsequent exploitation in molecular motors, which can perform useful work.

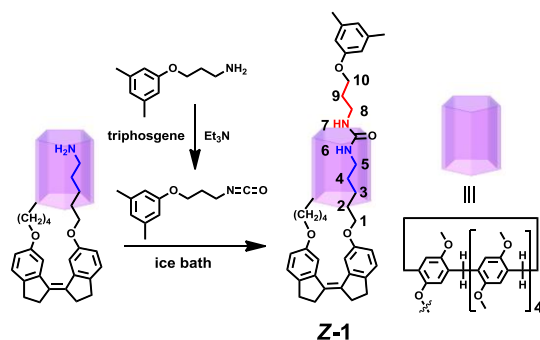
Light offers several advantages as a source of energy to power molecular machines: unlike chemical fuels it does not generate byproducts and can be introduced or withdrawn remotely.⁶ Optically-powered molecular motors can operate by a mechanism inaccessible for analogs that use only thermally-activated reactions.⁷ Light-driven rotary molecular machines, often based on *cis/trans* isomerization of overcrowded olefins, include examples that generate macroscopic work.⁸ Optically-triggered linear conformational motion has been achieved using rotaxanes containing a photoisomerizable group in the axle.^{1, 9} Photoisomerization of this moiety is exploited either to trigger the motion by changing the affinity of this group for the “wheel” or to block sterically translation of the “wheel” along the axle.¹⁰

Here we demonstrate an alternative approach for achieving light-powered translation of one molecular subunit relative to another (Scheme 1). For this proof-of-concept demonstration we used a rotaxane-like construct with stiff stilbene serving both as the photoisomerizable group that powers the translation of the pillar[5]arene “wheel” and as a stopper that prevents dethreading of the “wheel”. The motion is caused by the elongation or contraction of stiff stilbene upon its *E*->*Z* and *Z*->*E* photoisomerizations. This structural change is transduced into translation of the “wheel” by a linker connecting stiff stilbene and the “wheel”.



Scheme 1. A schematic presentation of the directed motion of the wheel triggered by photoisomerization of stiff stilbene. The blue (A) and red (B) rectangles represent two localization sites of the “wheel”.

Although stiff stilbene has never been incorporated in rotaxanes, it is an increasingly popular photoswitch recently used to control receptor affinity and twist angle of binaphthyl,¹¹ assembly of supramolecular polymers,¹² enantioselectivity of a catalyst¹³ and to model mechanochemical processes in polymers¹⁴. Rotary molecular motors capable of generating useful work have been created from chiral derivatives of stiff stilbene.¹⁵



Scheme 2. Synthesis of Z-1. See Scheme S1 for further details.

We assembled Z-1 by a nucleophilic addition reaction from two readily available components in 70% yield¹⁶ (Schemes 2 and S1) and verified the composition of the product by HR-MS spectroscopy (Fig. S1). A combination of 1D and 2D ¹H NMR spectra confirmed that in Z-1 the pillar[5]arene encapsulates the axle, localizing over its A region (Figs. 1, S2-S6 and S8-S10).

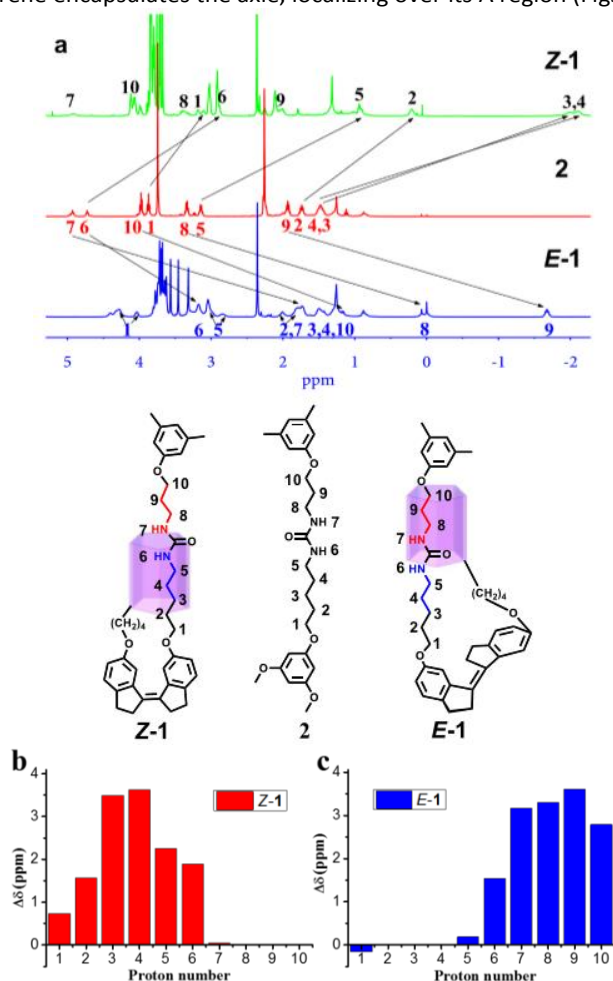


Fig. 1. (a) Partial ¹H NMR spectra (400 MHz, CDCl₃, 298 K) of rotaxanes Z-1, E-1 and of model axle 2. (b) The difference in the chemical shifts of the equivalent protons in model axle 2 and in Z-1. (c) The difference in the chemical shifts of the equivalent protons in model axle 2 and in E-1. The plotted data is tabulated in Tables S1-S2.

First, of the 10 protons of the axle in Z-1, only H1-H6 (A region) are shifted upfield compared to the equivalent protons of model axle 2. Such upfield shifts were previously demonstrated to indicate encapsulation of alkyl chains by pillar[5]arenes.^{17, 18} Second, a strong correlation between H1-H6 and the aromatic protons of pillar[5]arene was observed in the 2D NOESY spectrum of Z-1. We assigned chemical shifts of all protons for all compounds described here on the basis of their ¹H-¹H COSY spectra.

Irradiation of Z-1 at 387±5 nm in an anaerobic solution produces a photostationary state containing 90% of E-1 as determined by HPLC. The high fraction of the E isomer in the photostationary state results from the negligible extinction coefficient of the E (but not Z) isomer of stiff stilbene at these wavelengths.^{14a} The UV-vis (Fig. S11) and ¹H NMR spectra of the newly formed compound were consistent with the E isomer of stiff stilbene. The differences in ¹H NMR spectra of the two isomers of 1 indicate that Z→E photoisomerization of stiff stilbene was accompanied by translation of pillar[5]arene from the A to the B region of the axle (Figs.

1 and S13-S17). The chemical shifts of protons H1-H6 (A region), which in **Z-1** are shifted considerably upfield relative to those in model axle **2** are very similar in **E-1** and **2**. Conversely, protons H7-H10 (B region) appear at nearly identical chemical shifts in **Z-1** and **2**, but are shifted upfield by up to 3.6 ppm in **E-1**.

We repeated light-powered conversion between **Z-1** and **E-1** multiple times without accumulation of any detectable side products or changes in the composition of the photostationary states (Fig. 2).

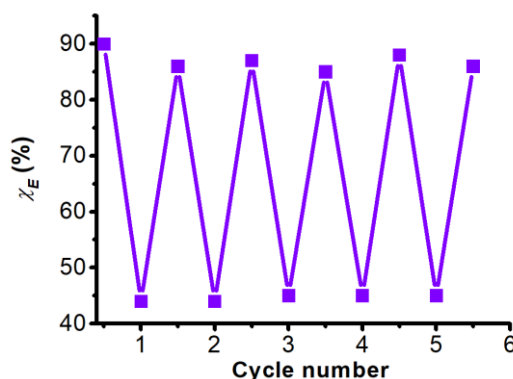


Fig. 2. Molar fraction of **E-1**, χ_E , in the photostationary states obtained by alternating the irradiation of an anaerobic solution of **1** between 387±5 nm (5 min to reach the photostationary state, half integer cycle numbers) and >360 nm (integer cycle numbers) for five complete cycles. The compositions of the states were confirmed by HPLC (Fig. S29). The light source was a xenon lamp with a 10-nm bandwidth or cutoff filters, for 387 and >360 nm, respectively.

Translation of pillar[5]arene from region A to region B of the axle upon **Z**→**E** isomerization of stiff stilbene occurs despite the fact that in the absence of stiff stilbene, localization of pillar[5]arene in region B is thermodynamically unfavorable over localization in region A. This conclusion is based on ^1H NMR studies of model compounds **3-5** (Fig. 3). Rotaxane **3** is similar to **1** except for the absence of stiff stilbene. The chemical shifts of the axle protons in **3** are very similar to those in **Z-1**: protons H1-H6 (region A) are shifted, relative to those of uncomplexed axle **2** (Fig. 1), by up to 3.6 ppm upfield, while protons H7-H10 (region B) occur at nearly the same chemical shifts as in **2** (maximum difference of 0.035 ppm for H10, Figs. S19-S22, S30 and Table S3).

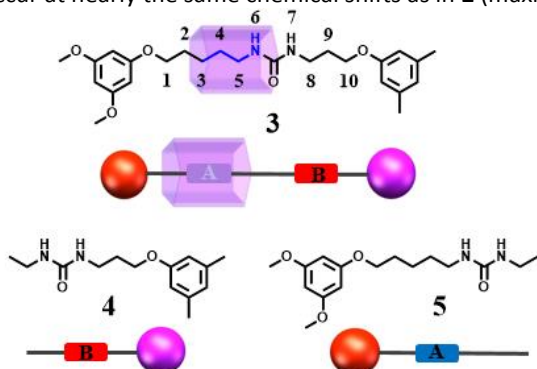


Fig. 3. Model compounds **3-5**.

The nearly identical chemical shifts of proton of the B region in **2**, **3** and **Z-1** indicate that at 300 K <10% of the molecules of **Z-1** and **3** contain pillar[5]arene over the B region of the axle, corresponding to >1 kcal mol⁻¹ difference in binding affinities of pillar[5]arene for these two regions of the axle. To improve this estimate we measured the association constants between pillar[5]arene and half-axes **4** and **5** by ^1H NMR titration (Figs. S31-34).¹⁹ The obtained values (23 ± 3 M⁻¹ for pillar[5]arene•**4** and 126 ± 5 M⁻¹ pillar[5]arene•**5**) correspond to the difference of the standard free energies of association of 1.0 kcal mol⁻¹ in favor of the A region.

To characterize the structural and energy differences associated with **E/Z** photoisomerization of stiff stilbene in **1** we optimized all conformers of **E-1**, **Z-1** and **3** at the B3LYP/6-31G(d)//CAM-B3LYP/6-31+G(d) level of DFT in vacuum. These calculations accurately reproduced the measured 1 kcal mol⁻¹ preference of pillar[5]arene for region A in **3**, giving credence to the calculated relative energies of the isomers of **1**. Fig. 4 illustrates the optimized minimum-energy conformers of **1** with pillar[5]arene localized in the A and B regions and both isomers of stiff stilbene. The calculations allow us to draw three conclusions that would be useful in guiding further elaborations of the reported molecular architecture.

First, the calculated difference in the electronic energies of **Z-1** and **Z-1'** (Fig. 4) is identical to that of **3** with the “wheel” localized at A and B (Fig. S35) suggesting that linking **Z** stiff stilbene to pillar[5]arene does not perturb the intrinsic preference of pillar[5]arene for the A region of the axle.

Second, the energy difference between **E-1'** and **E-1** (10 kcal mol⁻¹, Fig. 4) places the upper limit on the useful work that could be extracted from a molecular motor based on the same molecular architecture and chemical interactions as **1**. Although this upper limit can be increased by using an axle of two A regions (instead of A+B architecture of **1**), in the **Z** isomer of such a derivative pillar[5]arene would equipartition between the two regions, which may be undesirable.

Third, isomerization of stiff stilbene causes translation of pillar[5]arene by 1.1 nm (relative to the C=O group of the axle). This distance is over twice the difference in the separation of the O atoms connecting stiff stilbene to the rest of the molecule in its two isomers. The fact that the “wheel” moves by more than stiff stilbene, which causes the translation, elongates reflects the conformational flexibility of the axle that accommodates very different orientations of the two isomers of stiff stilbene relative to the rest of the molecule. This flexibility means that stiff stilbene does not constrain the magnitude of the “wheel” motion, which appears to be determined by the separation of the moieties of the axle that form favourable interactions with the “wheel” (in this case, hydrogen bonding between NH and PhOMe groups). Replacing the urea moiety of **1** by oxamide, dithioamide or 2,2-dimethylpropanediamide groups may increase the magnitude of light-triggered motion up to 1.7 nm. We are currently pursuing such modifications to understand broad correlations between the shuttling distance, its energetics and kinetics in the molecular architecture introduced here.

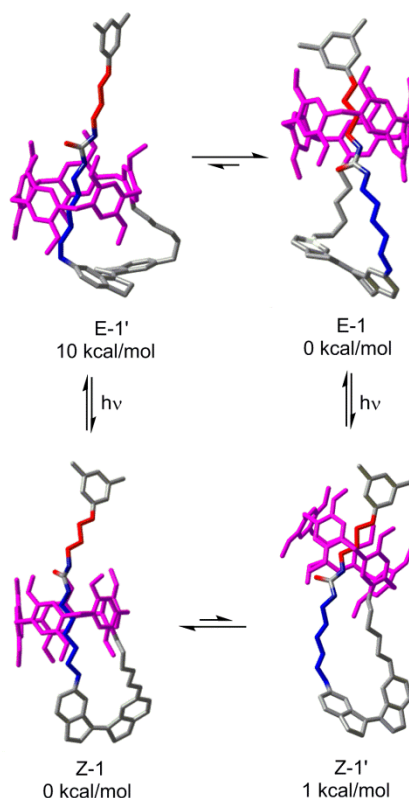


Fig. 4. Calculated molecular geometries and the relative energies of the minimum-energy conformers of **1** for the two isomeric states of stiff stilbene (CPK color) and the two locations of the “wheel” (magenta) along the axle (A region in blue, B region in red). H atoms are omitted for clarity.

The molecular architecture of **1** may make it a useful platform to study how external loads affect the efficiency of molecular photomechanical energy conversion by altering the relative contributions of the two limiting transduction mechanisms: the power stroke (exemplified in **1** by the $Z\text{-}1 \rightarrow E\text{-}1' \rightarrow E\text{-}1$ path, Fig. 4) vs. the ratchet ($Z\text{-}1 \rightarrow Z\text{-}1' \rightarrow E\text{-}1$).^{7,20-22} For example, coupling translation of the “wheel” from station A (closest to stiff stilbene) to station B against an external load (e.g., using the methods we previously described),^{14a} would destabilize $Z\text{-}1'$ intermediate and bias the isomerization toward the power stroke mechanism. However, such load may also affect the quantum yields of isomerization in a manner that cannot be at present predicted quantitatively.²² The molecular architecture of **1** and the favorable photophysics of stiff stilbene isomerization²² allow these questions to be systematically studied by measuring the rate of $Z\text{-}1 \rightarrow E\text{-}1$ isomerization against an external load as a function of the photon flux and reaction temperature, as previously described.^{14a}

In summary, we demonstrated a new molecular design for optically triggered nm-scale translation of a molecular subcomponent relative to another. We used a rotaxane-like molecule terminated at one end with stiff stilbene that served both as a chromophore to trigger the translation of the pillar[5]arene “wheel” and as a stopper to prevent its dethreading. An important advantage of the architecture of **1** is that the functions of the chromophore, the “wheel” recognition sites and their separator are all performed by distinct molecular moieties (i.e., stiff stilbene, NH groups and C=O, respectively in the current implementation), allowing any to be modified independently of the others while preserving large-scale conformational motion. Since the relationship between the molecular structure and the performance characteristics (energy conversion efficiency, stall force, power output) of synthetic molecular motors is poorly understood,^{20,22} such design flexibility is likely to be valuable both for identifying broad structure/performance relationships of molecular photomechanical energy conversion and for optimizing the structure of a motor to fit a particular task.

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Conflicts of interest

There are no conflicts to declare.

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